

CLAIMS

What is claimed is:

Subj 1 ~~1. An isolated nucleic acid molecule comprising a sequence substantially equivalent to that of SEQ ID NO: 1 or a fragment thereof having at least about 40 nucleotides.~~

- ~~1. An isolated nucleic acid molecule comprising a sequence substantially equivalent to that of SEQ ID NO: 1 or a fragment thereof having at least about 40 nucleotides.~~
2. A recombinant vector comprising the nucleic acid molecule of claim 1.
3. A genetically engineered cell comprising the recombinant vector of claim 2.
- ~~4. An isolated polypeptide comprising an amino acid sequence substantially equivalent to that of SEQ ID NO: 2 or a fragment thereof.~~
5. The isolated polypeptide of claim 4 further comprising a purification domain.
6. The isolated polypeptide of claim 5 wherein said purification domain is gluathione-S-transferase.
7. The isolated polypeptide of claim 4 further comprising a DNA binding domain.
8. The isolated polypeptide of claim 7 wherein said DNA binding domain is the Gal4 DNA binding domain.
9. The isolated polypeptide of claim 4 further comprising a transcription activation domain.
10. The isolated polypeptide of claim 9 wherein said transcription activation domain is the Gal4 transcription activation domain.
11. The isolated polypeptide of claim 4 wherein said peptide substantially lacks methyltransferase activity, but retains the ability to bind to p160 proteins.

12. The isolated polypeptide of claim 11 wherein the substitution of residues 189, 190, and 191 of SEQ ID NO: 2 result in the substantial lack of methyltransferase activity and retention of p160 binding ability.

13. The isolated polypeptide of claim 12 which has the amino acid sequence of SEQ ID NO: 3 or a fragment thereof.

14. An antibody directed towards the isolated polypeptide of claim 4.

15. The antibody of claim 14 wherein said antibody is monoclonal.

16. The antibody of claim 14 wherein said antibody is polyclonal.

17. A method for methylating amino acid residues within a substrate polypeptide comprising contacting the polypeptide of claim 4 with said substrate polypeptide in the presence of S-adenosylmethionine.

18. The method of claim 17 wherein said substrate amino acid residue that is methylated is arginine.

19. The method of claim 17 wherein said substrate polypeptide is a histone.

20. The method of claim 19 wherein said histone is histone H3.

21. A methylated histone H3 or fragment thereof produced according to the method of claim 17.

22. An antibody directed towards the methylated histone of claim 21.

23. A method for screening for molecules that modulate an interaction between CARM1 and GRIP-1 comprising:

expressing within a host cell a first recombinant protein comprising SEQ ID NO: 2 or a fragment thereof fused to a first interaction domain;

expressing within said host cell a second recombinant protein comprising a CARM1-interacting protein or fragment thereof fused to a second interaction domain;

providing in said host cell a reporter gene construct comprising a reporter gene and a promoter region which interacts with either said first interaction domain or said second interaction domain and wherein said first recombinant protein and said second recombinant protein interact with sufficient affinity to facilitate expression of said reporter gene; and

measuring said reporter gene expression level in the presence of a modulating molecule.

24. The method of claim 23 wherein said first interaction domain is a DNA binding domain and said second interaction domain is a transcriptional activation domain.

25. The method of claim 23 wherein said first interaction domain is a transcriptional activation domain and said second interaction domain is a DNA binding domain.

26. The method of claim 23 wherein said reporter gene construct comprises a nucleic acid molecule encoding β -galactosidase, green fluorescent protein, luciferase or β -lactamase.

27. A method for modulating expression of a nuclear receptor-dependent gene in a cell comprising:

expressing in said cell a first nucleic acid molecule encoding a protein arginine methyltransferase;

expressing in said cell a second nucleic acid molecule encoding a p160 coactivator; and

wherein the co-expression of said first and said second nucleic acid molecules modulates the expression level of said nuclear receptor-dependent gene.

28. The method of claim 27 wherein said protein arginine methyltransferase is CARM1, PRMT1, PRMT2 or PRMT3.

29. The method of claim 28 further comprising expressing a second protein arginine methyltransferase.

30. The method of claim 29 wherein said first protein arginine methyltransferase is CARM1.

31. The method of claim 30 wherein said second protein arginine methyltransferase is PRMT1, PRMT2 or PRMT3.

32. The method of claim 28 further comprising expressing a second coactivator wherein said second coactivator possesses histone acetyltransferase activity.

33. The method of claim 32 wherein said second coactivator is CBP, P/CAF or p300.

34. A method for screening of molecules that modulate CARM1 coactivator activity in a cell comprising:

expressing in said cell a nuclear receptor-dependent reporter gene;

expressing in said cell CARM1;

expressing in said cell a p160 coactivator;

expressing in said cell a second coactivator with histone acetyltransferase activity or a second protein arginine methyltransferase;

expressing in said cell a nuclear receptor gene, wherein said nuclear receptor gene is expressed at a level such that expression of said reporter gene is at least about 10-fold higher than in a cell not expressing either CARM1, a p160 coactivator, or either a second coactivator or a second protein arginine methyltransferase; and

comparing the expression levels of said reporter gene in said cell in the presence and absence of a modulating compound.

35. The method of claim 34 wherein said p160 coactivator is GRIP1, SRC-1 or p/CIP.
36. The method of claim 35 wherein said p160 coactivator is GRIP1.
37. The method of claim 35 wherein said second coactivator is p300, CBP or p/CAF.
38. The method of claim 35 wherein said second protein arginine methyltransferase is PRMT1, PRMT2 or PRMT3.

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